Remarks

Further and favorable reconsideration is respectfully requested in view of the foregoing amendments and following remarks.

Thus, claim 1 has been amended to incorporate the subject matter of claim 6, limiting the water-soluble polymer to sodium polyacrylate, as a result of which claim 6 has been cancelled.

Amended claim 1 also recites that the preparation has an ointment form before its use and protects the wound, by transformation from a sol to a gel during use, with easy separation of the gel substantially as a mass after its use, which is supported by the disclosure at page 6, line 15-25 of the specification.

Claim 2 has been amended to limit the water-soluble polymer to sodium polyacrylate, consistent with this amendment to claim 1.

Claim 15 has been amended to insert the same language as inserted at the end of amended claim 1.

Applicants respectfully submit that these amendments should be entered, even though they are presented after a final rejection. As indicated above, claim 6, which has already been considered by the Examiner, has been incorporated into claim 1, and therefore, this amendment will not require any further consideration and/or search. The language concerning the transformation of the preparation from a sol to a gel during use, with easy separation of the gel substantially as a mass after its use, inserted into claims 1 and 15, was not previously submitted because it is responsive to the Examiner's position as set forth in the third paragraph on page 2 of the Office Action.

The patentability of the presently claimed invention after entry of the foregoing amendments over the disclosures of the references relied upon by the Examiner in rejecting the claims will be apparent upon consideration of the following remarks.

Thus, the rejection of claims 1, 2, 6, 7 and 13-16 under 35 U.S.C. § 103(a) as being unpatentable over Mizobuchi et al. (WO'651/US'355) in view of Knutson (US'651) is respectfully traversed. [Please note that claim 14 was previously cancelled.]

In the last paragraph on page 2 of the Office Action, the Examiner states that Applicants argue that the composition of Mizobuchi et al. "is already in sol state prior to use". However, to the contrary, and referring to page 5, lines 14-16 of Applicants' response filed January 27, 2010,

Applicants have argued that the Mizobuchi et al. "preparation is already in a **gel** state prior to use".

Also on page 2 of the Office Action, the Examiner notes that the instant claims do not require the **preparation** to be in a sol state, but the water-soluble polymer. However, referring to the amendment at the end of each of claims 1 and 15, the **preparation** is transformed from a sol to a gel during use.

Referring to the Examiner's comments in the first full paragraph on page 5 of the Office Action, and as noted above, independent claim 1 has now been amended to limit the water-soluble polymer to sodium polyacrylate. With regard to the crosslinking agents, sugars and fluidization agents, Applicants take the position that the Examiner has offered no reason to expect that crosslinking agents, sugar and fluidization agents other than those in the data previously presented by Applicants would not produce similar results.

Comparison with Mizobuchi et al.

1) Formulation of Mizobuchi et al.

In the previous Office Action, the Examiner referred to the formulation of Example 25 in Table 4 of Mizobuchi et al. as the closest prior art to the present invention. This formulation has been prepared, and it has been confirmed that it is easily gelated to give a gel state composition.

Thus, as shown in the attached Declaration of the inventor, Mr. Hamamoto, the formulation of Example 25 was completely gelated at room temperature to give an elastic mass.

2) Claimed formulation

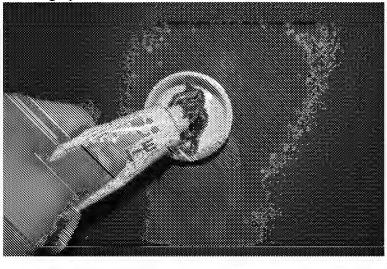
As recited in claim 1, a formulation of the present invention is an ointment with a sol state. Also, a commercial product of the present invention, having ingredients similar to Preparation No. 4 of the present application (Table 2 on page 24) was already launched (August 2005) on the market in Japan as "Iodocoat® Ointment 0.9%" (See attached Exhibit 1 translation):

Ingredients	Preparation No. 4	Commercial product "Iodocoat® Ointment":
sodium polyacrylate	14	14
carmellose sodium	10	6
aluminium lactate		
magnesium aluminometasilicate	1	ca.1
synthetic hydrotalcite	0.1	0.1
white soft sugar	10	10
potassium iodide	1	ca.1
malic acid	1.4	1.4
tartaric acid	2	ca.2
iodine	1	ca.1
macrogol	residue(ca.60)	residue(ca.60)

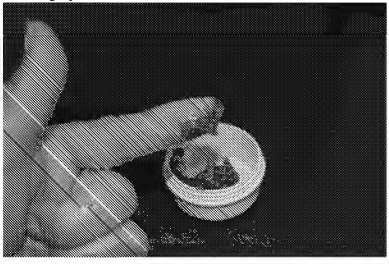
3) Comparison with Mizobuchi et al.

The commercial product of the present invention is an ointment with a **sol state** as shown in <Photograph 1>, and it is possible to apply it to a wounded site with your fingertip <Photograph 2>. However, the formulation of Mizobuchi et al. is an **elastic solid** <Photograph 3> and it is impossible to spread it on the skin.

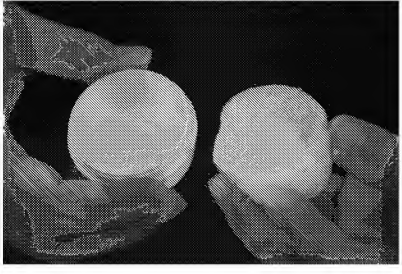
<Photograph 1>



<Photograph 2>

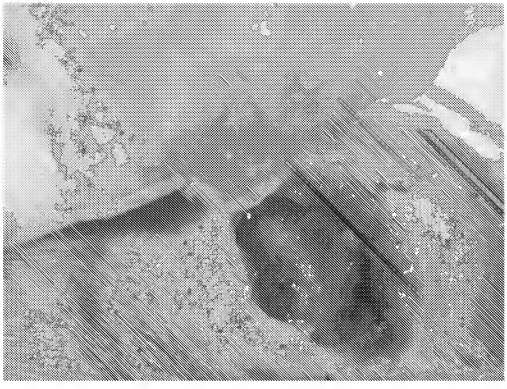


<Photograph 3>

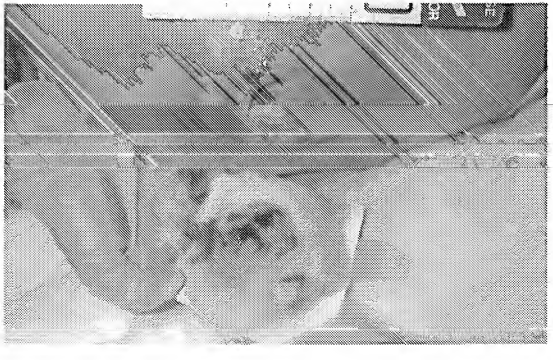


Feature of gelation in the present invention

One of the characteristics of the present formulation is that it has a superior property of "easy separation of the gel substantially as a mass after its use." For example, the present formulation was applied to a wound of a burn model in a rat (150 mg/day) and covered with a gauze. The formulation was gelated by absorbing exudates and could be removed as a mass as shown in the next picture 5 days later.



Further in the next picture, it is demonstrated that the commercial product of the present invention is applied to a bedsore and after 24 hours the gelated ointment is removed as a mass together with a gauze.



With respect to Applicants' argument that the present invention has a superior property of being easily separated after use, the Examiner states that the present invention has not been compared to the closest prior art. As demonstrated in the attached Declaration, however, the formulation of Mizoguchi et al. is easily gelated prior to use to give a solid composition, and it is not possible to spread it on the wounded surface.

Effect of the present invention

As mentioned above, a formulation of the present invention is already launched on the market in Japan and the therapeutic effects are reported as follows (see attached Exhibit 2 translation):

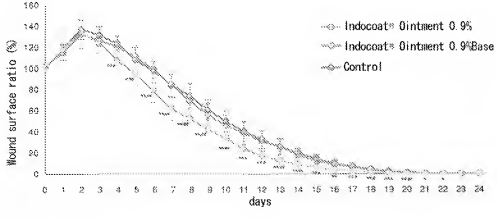
a) Treatment effect in a rat burn model [1)]

Method: A test medicine was applied in an amount of 150 mg/once a day to a rat experimental burn model, which corresponds to a burn wound of degree III [2)]. Transient ratio of wound surface and days for treatment were observed until epithelization was completed. As a control, a gauze soaked in sterile physiological saline was applied.

1) a rat experimental burn model: The back of a rat was dehaired, and a burn wound was evoked by pressing a heated iron under anesthesia. Dead skin was surgically removed 2 days after evoking the burn wound.

2) a burn wound of degree III: a model in which heat denaturation reached to the subcutaneous tissue.

[Wound surface ratio*] :



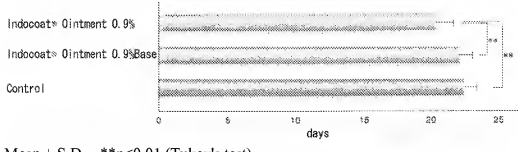
*wound surface ratio(%) =

$$\frac{\text{(long diameter x short diameter on a day of measure)}}{\text{(long diameter x short diameter on a day of starting administration)}} \times 100$$

Mean ± S.D. *p<0.05, **p<0.01 (vs. control group, Tukey's test)
n=10 #p<0.05, ##p<0.01 (vs. Iodocoat® Ointment 0.9% Base, Tukey's test)

In a group of Iodocoat® Ointment 0.9%, a significant reduction of wound surface ratio was observed on 4 to 22 days compared to a control group. A significant reduction of wound surface ratio was also observed on 4 to 15 and 17 to 21days compared to a group of Iodocoat® base.

[Days for treatment] :



Mean ± S.D. **p<0.01 (Tukey's test)
n=10

In a group of Iodocoat® Ointment 0.9%, a significant reduction of days for treatment was observed compared to a control group or a group of Iodocoat® base.

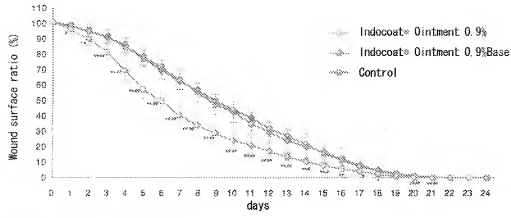
b) Treatment effect in a rat bedsore model [1)]

Method: A test medicine was applied in an amount of 150 mg/once a day to a rat experimental bedsore model, which corresponds to a bedsore of degree III. Transient ratio of wound surface and days for treatment were observed until epithelization was completed. As a control, a gauze soaked in sterile physiological saline was applied.

1) a rat bedsore model: The back of a rat was dehaired, and loaded under pressure for 24 hours under anesthesia. Dead skin was surgically removed 2 days after pressure was removed.

2) a bedsore of degree III: a model in which denaturation reached to the fatty tissue, but not to the muscle membrane.

[Wound surface ratio*] :



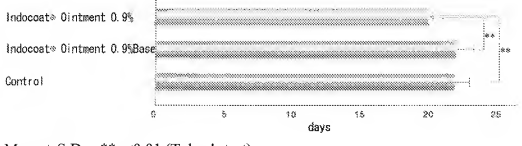
*wound surface ratio(%) =

$$\frac{\text{(long diameter x short diameter on a day of measure)}}{\text{(long diameter x short diameter on a day of starting administration)}} \times 100$$

Mean ± S.D. *p<0.05, **p<0.01 (vs. control group, Tukey's test)
n=10 #p<0.05, ##p<0.01 (vs. Iodocoat® Ointment 0.9% Base, Tukey's test)

In a group of Iodocoat® Ointment 0.9%, a significant reduction of wound surface ratio was observed on 2 to 16, 18, 20 and 21 days compared to a control group. A significant reduction of wound surface ratio was also observed on 1 to 15 and 17, 20 and 21days compared to a group of Iodocoat® base.

[Days for treatment] :



Mean ± S.D. **p<0.01 (Tukey's test)
n=10

In a group of Iodocoat® Ointment 0.9%, a significant reduction of days for treatment was observed compared to a control group or a group of Iodocoat® base.

It is therefore apparent that the presently claimed preparation is clearly distinct from, and not suggested by, the Mizobuchi et al. reference.

The Examiner applies the Knutson reference for its disclosure of wound healing agents such as sugar and povidone-iodine, taking the position that it would be obvious to add these ingredients to the ointment composition of Mizobuchi et al. However, even if these ingredients were added to the Mizobuchi et al. composition, it is apparent that the result would still be very different from the presently claimed invention in view of the distinctions between the present invention and Mizobuchi et al. as discussed above.

For these reasons, Applicants take the position that the present invention is clearly patentable over the applied references.

Therefore, in view of the foregoing amendments and remarks, it is submitted that the ground of rejection set forth by the Examiner has been overcome, and that the application is in condition for allowance. Such allowance is solicited.

Respectfully submitted,

Hidetoshi HAMAMOTO et al.

Digitally signed by /Michael R. Davis/
DN: cn=/Michael R. Davis/, o=WLP, ou, email=mdavis@wenderoth.com, c=US
Date: 2010.10.13 15:51:49 -04'00'

By /Michael R. Davis/

Michael R. Davis
Registration No. 25,134
Attorney for Applicants

MRD/mac
Washington, D.C. 20005-1503
Telephone (202) 721-8200
Facsimile (202) 721-8250
October 13, 2010